UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

March 24, 2000

MEMORANDUM

SUBJECT: OXAMYL. The **Revised** HED Chapter of the Reregistration Eligibility Decision Document (RED). PC Code: 103801. Case # 0253. DP Barcode: D263842.

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Attached please find the revised Health Effects Division's (HED's) risk assessment for oxamyl. This document takes into consideration comments made by the registrant during the 30-day error correction period (Phase 1) of the public participation process. For the revised assessment, anticipated residue estimates for pineapple and apple, and processing factors for baked and canned food forms, were reassessed. Minor changes have been made to the product chemistry, toxicology, residue chemistry, and occupational exposure chapters to reflect comments made by DuPont in Phase 1. A list of the disciplinary science chapters and other supporting documents that are included as attachments can be found at the end of this document.

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1.0 EXECUTIVE SUMMARY

The Agency has conducted a human health risk assessment for the active ingredient oxamyl (methyl N',N'-dimethyl-N-[(methylcarbamoyl)-oxy]-1-thiooxamimidate), for the purpose of making a reregistration eligibility decision. Oxamyl is a carbamate insecticide, acaricide, and nematocide that controls a broad spectrum of insects, mites, ticks, and roundworms on various field crops, vegetables, fruits, and non-bearing trees. There are no registered residential uses of oxamyl. Oxamyl is registered by DuPont de Nemours (DuPont) under the trade name of Vydate®, and is formulated as a soluble concentrate/liquid (24 percent and 42 percent active ingredient) and as a liquid technical (42 percent active ingredient).

Oxamyl is classified by the EPA as a restricted-use pesticide and may be purchased and used only by certified applicators. Oxamyl may work both through systemic distribution in the target pest and on contact. Oxamyl can be applied directly to plants or to the soil surface.

The critical toxic endpoints selected for risk assessment purposes are based primarily, but not exclusively, on cholinesterase inhibition (ChEI) in the brain, red blood cell, and plasma, as well as systemic toxicity (decreased body weight gains). Oxamyl is classified as a Group E carcinogen (not likely to be carcinogenic) based on a lack of carcinogenicity found in studies on male and female mice, as well as in male and female rats.

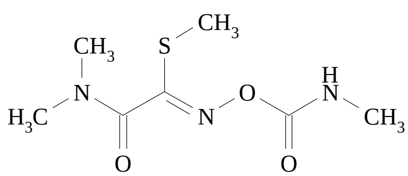
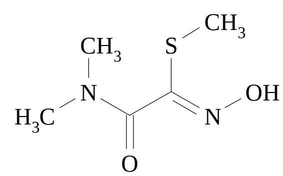
An uncertainty factor (UF) of 100X was applied to the risk assessment to account for interspecies extrapolation and intraspecies variability. The FQPA safety factor for the protection of infants and children (as required by the Food Quality Protection Act of August 6, 1996) was reduced to 1X for the acute and chronic dietary risk assessments. A Margin of Exposure (MOE) of $\geq$100 is considered to be below the Agency's risk of concern for occupational exposure scenarios.

Tolerances for oxamyl are expressed as the sum of the residues of the parent oxamyl and its oxime metabolite (N',N'-dimethyl-N-hydroxy-1-thiooxamimidate), calculated as oxamyl in or on raw agricultural commodities (RAC). The Metabolism Assessment Review Committee (MARC) has determined that oxime is not likely to be a potent acetyl cholinesterase inhibitor. It is not possible to exclude oxime from the tolerance expression as analytical methods used for field trial and enforcement typically convert oxamyl to oxime. This differs from pesticide monitoring programs which employ methods that allow for quantitation of both entities (J. Punzi memo, 11/18/99).

The dietary exposure is based on ChE inhibition by parent (oxamyl) only, however, field trial data used for the dietary exposure assessment do not distinguish between the parent oxamyl and the oxime metabolite. Therefore, the exposure contribution from raw agricultural commodities based on field trials may be overestimated. On the other hand, the United States Department of Agriculture's Pesticide Data Program (PDP) and the Food and Drug Administration (FDA) data, which do distinguish between the parent oxamyl and the oxime metabolite, were also used in this assessment. The levels of oxamyl *per se* are reported and thus use of this data will more accurately reflect exposure contribution.

The Agency has determined that there is no reasonable expectation of finite oxamyl residues in animal commodities; consequently, there are no tolerances for meat, milk, poultry, or eggs. The published tolerances range from 0.1 ppm (potatoes and various root crops) to 10 ppm (peppermint and spearmint hay, and pineapple forage). The reassessed tolerances are listed in the attached Revised Residue Chemistry Chapter (J. Punzi memo, 03/07/00).

Figure A. Chemical structures of oxamyl and its oxime metabolite.

Oxamyl: methyl N',N'-dimethyl-N-[(methylcarbamoyl)-oxy]-1-thiooxamimidate	**Oxime metabolite**: methyl N',N'-dimethyl-N-hydroxy-1-thiooxamimidate
	

The acute and chronic dietary risk assessments for oxamyl are highly refined (Tier 3) analyses that incorporate percent crop treated information and monitoring data from PDP and FDA surveillance data. The chronic dietary analysis indicates no risk of concern for any population subgroup, with a chronic dietary risk estimate of 12% of the chronic Population Adjusted Dose (cPAD)[1] for the highest exposed population subgroup (children 1-6 years old). The acute dietary analysis indicates no risk of concern for any population subgroup, with an acute dietary risk estimate of 81% of the aPAD for the highest exposed population subgroup (children 1-6 years old). Calculated risks are based on acute and chronic PADs of 0.001 mg/kg/day.

Potential exposures and risks from oxamyl residues in drinking water were assessed using modeling techniques (Tier 2 PRZM/EXAMS for surface water) and monitoring data for ground water. The drinking water assessment only samples for the parent oxamyl. For risk assessment purposes, surface water estimated environmental concentrations (EECs) of oxamyl are 1.0 ppb (acute) and 0.3 ppb (chronic). Groundwater EECs are based on monitoring data and are calculated as 5 ppb (acute) and 1 ppb (chronic). Acute exposure to residues of oxamyl in drinking water may be a risk of concern for children 1-6 years old. Chronic exposure to residues of oxamyl in drinking water do not result in an unacceptable contribution to dietary exposure.

The Agency has determined that there are potential exposures to mixers, loaders, applicators, and other handlers during usual use-patterns associated with oxamyl. The Agency has identified eight major exposure scenarios for oxamyl: (1a) mixing/loading liquids for aerial application; (1b) mixing loading liquids for groundboom application; (1c) mixing/loading liquids for airblast application; (1d) mixing/loading liquids for spotgun applicator; (1e) mixing/loading liquids for high pressure handwand application; (2) applying liquids with aerial equipment; (3) applying

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[1] PAD = Population Adjusted Dose $= \dfrac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

liquids with a groundboom sprayer; (4) applying liquids with an airblast sprayer; (5) applying liquids for spotgun treatment; (6) applying liquids with a high pressure handwand; (7) mixing/loading/applying liquids by seed piece dip; and (8) flagging for liquid aerial applications.

Calculations of risk based on combined dermal and inhalation exposure indicate that the MOEs are **more than 100** with maximum risk reduction measures (personal protective equipment (PPE) or engineering controls) for all of the short- and intermediate-term occupational exposure scenarios listed above **except** for the following: applying liquids with a spotgun applicator (MOE = 63); applying liquids with a high pressure handwand (MOE = 41); mixing/loading liquids for aerial and chemigation application for all application rates (MOEs range from 50-66); and applying liquids with aerial equipment for all application rates (MOEs range from 75-85). Inhalation exposure is the main contributor to overall occupational exposure. There are no available data to assess the exposure scenario mixing/loading/applying liquids by a seed piece dip (scenario 7).

The Agency has determined that there are potential exposures to post-application workers during usual use-patterns associated with oxamyl. Three studies were conducted in support of oxamyl reregistration. The dislodgeable foliar residue (DFR) studies were conducted on cucumbers, tomatoes, and citrus fruits. Two sites were chosen for each crop: one in California, and one in either Florida or Georgia, to represent an arid and a non-arid climate. A soil residue dissipation study was also conducted on tomatoes at the California site.

The calculated or target MOE of $\geq$100 is achieved for cucumbers on day four at the California site and on day one at the Georgia site. The calculated MOE of $\geq$100 for citrus trees is achieved on day three at the Florida site and on day seven at the California site. For tomato foliage, the calculated MOE of $\geq$100 is achieved on day four for the Florida site and on day three for the California site. Target MOEs for all other crops were assessed using the DFR data as surrogate data. The current labels for oxamyl list the restricted entry interval (REI) as 48 hours. The transfer coefficients used to calculate the day after application when the MOE exceeds 100 are standard Agency default values, and range from 2,500 cm^2/hr to 10,000 cm^2/hr.

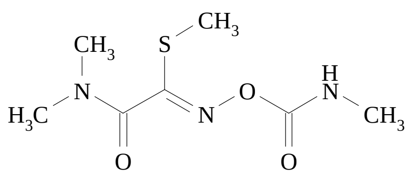
As mandated by the FQPA amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA), the Agency must consider total aggregate exposure from food, drinking water, and residential sources of exposure to oxamyl. Since oxamyl has no registered residential uses, this aggregate assessment will only consider exposure to oxamyl from food and drinking water. Acute exposure to residues of oxamyl in food is below the Agency's level of concern (< 100% aPAD). However, residues of oxamyl in drinking water may result in an unacceptable acute aggregate risk estimate. Chronic exposure through food and drinking water sources are below the Agency's level of concern (<100% cPAD). Therefore, the Agency concludes with reasonable certainty that residues of oxamyl in drinking water (when considered along with exposures from food uses) would not result in an unacceptable chronic aggregate human health risk estimate.

The Agency is in the process of formulating guidance for conducting cumulative risk assessment. When the guidance is finalized, oxamyl and other ChE-inhibiting compounds (carbamates and organophosphates) will be revisited to assess the cumulative effects of exposure to multiple cholinesterase-inhibiting compounds.

Risk estimates of residential dermal and inhalation exposures were not estimated, as there are no registered residential uses of oxamyl. The Agency has concerns about possible residential risks from oxamyl spray drift. The Agency is currently developing methods to assess residential risks from spray drift, and these risks will be assessed in the future when new methods are available.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Oxamyl [methyl N',N'-dimethyl-N-((methylcarbamoyl)-oxy)-1-thiooxamimidate] is an insecticide/nematicide/acaricide registered for use on various field crops, vegetables, fruits, and ornamentals.



Empirical Formula:	$C_7H_{13}N_3O_3S$
Molecular Weight:	219.3
CAS Registry No.:	23135-22-0
PC Code:	103801

Oxamyl is a white crystalline solid with a slight sulfurous odor. Oxamyl "melts" at 97-100 C where it changes to a different crystalline form which melts at 108-110 C. The vapor pressure is 3.84×10^{-7} mm Hg at 25 C. Oxamyl is soluble in water (28 g/100 g), methanol (130 g/100 g), acetone (67 g/100 g), ethanol (33 g/100 g), and toluene (1 g/100 g) at 25 C. Oxamyl is stable in solid form and as a liquid formulation, and is stable in aqueous solutions at pH 5 or lower, but hydrolyzes rapidly at pH 9.

Additional data pertaining to OPPTS Guidelines 830.1600 (description of materials used to produce the product) and 830.7050 (UV/visible absorption) are required to satisfy product chemistry data requirements for the DuPont oxamyl technical grade active ingredient (TGAI) and formulation intermediate (FI). Provided that the registrant submits the data that is required in the Revised Product Chemistry Chapter (K. Dockter memo, 03/15/00) for the oxamyl TGAI and FI, and either certifies that the suppliers of beginning materials and the manufacturing process for the oxamyl manufacturing-use product have not changed since the last comprehensive product chemistry review, or submits a complete updated product chemistry data package, the Agency has no objections to the reregistration of oxamyl with respect to product chemistry data requirements.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

The toxicological database for oxamyl is complete and will support reregistration. In summary, oxamyl is acutely toxic via the oral and inhalation routes of exposure (toxicity categories I and II, respectively). Dermal toxicity is low, with a toxicity category of IV. Oxamyl is a mild eye irritant, and is not a skin sensitizer or a skin irritant in animal studies.

In an acute neurotoxicity study in rats, neurobehavioral effects [Functional Observational Battery (FOB) findings and numerous clinical signs] were observed at a dose level of 0.75 mg/kg/day (females) and 1 mg/kg/day (males). In the dietary subchronic neurotoxicity study, the same types of findings were observed at higher doses in males (14.9 mg/kg) and in females (19.9 mg/kg) with a no observed adverse effect level (NOAEL) of 2.1 mg/kg (males). The chronic dog and rat studies yielded a higher NOAEL/LOAEL as compared to the acute neurotoxicity study (dog NOAEL = 0.9 mg/kg, LOAEL = 1.36 mg/kg; rat NOAEL = 1.97 mg/kg, LOAEL = 4.19 mg/kg). ChEI was not measured at the peak time in chronic studies (dog 2-3 hours post feeding; rat study RBC and plasma at 1, 3, 6, 12, 18, and 24 months and brain ChE levels at 12 and 24 months from the 16 hour fasted animals).

Neurotoxic effects were also seen in maternal animals in the rat developmental toxicity study and in chronic dog studies. No neuropathological findings were associated with neurotoxicity effects in the above mentioned studies, except retinal photoreceptor cell atrophy, seen in females in a 2-year chronic rat study, which was considered within historical background and due to aging of the rats.

Systemic toxicity related to blood and brain ChE inhibition was observed in females at the highest dose tested (75 mg/kg) in a 21-day rabbit dermal toxicity study. No developmental toxicity was seen at the highest dose tested (4 mg/kg) following *in utero* exposure in rabbits.

Following *in utero* exposure in rats, decreased fetal body weights were seen in the presence of maternal toxicity. The apparent quantitative difference in susceptibility demonstrated in the prenatal developmental toxicity study in rats (developmental NOAEL of 0.2 mg/kg/day is quantitatively lower than the maternal NOAEL of 0.5 mg/kg/day) was not a true indication of increased susceptibility since a decrease in maternal body weight (not statistically significant) also occurred at the 0.5 mg/kg/day dose (developmental LOAEL). In addition, at higher doses the decreases in fetal body weights corroborated with decreases in maternal body weights and food consumption and clinical signs with increasing doses. Thus, the data indicate that the decreases in fetal weights are not an indication of increased susceptibility, but occurred due to maternal toxicity.

In the two-generation reproduction study, offspring toxicity was seen only in the presence of parental/systemic toxicity at the highest dose tested (5.2 mg/kg). Therefore, there was no indication of increased susceptibility to offspring or pups following exposure to oxamyl.

No evidence of carcinogenicity was seen in any study. Oxamyl is classified as a “Group E” carcinogen because there was no evidence of carcinogenicity in male and female mice as well as male and female rats. Oxamyl is characterized as "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is supported by the lack of mutagenic activity (Memorandum: Report of the Hazard Identification Assessment Review Committee, Guruva Reddy, 08/31/99).

A radiolabelled dermal absorption study (MRID 40370101 & 41077601) is classified as **unacceptable** because the gauze covering had taken up most of the radioactivity and prevented much of the applied dose from being in contact with skin. The data derived from this study suggest that oxamyl is slowly absorbed through the skin (MRID 40370101 & 41077601). However, a dermal absorption factor is not required since route-specific short- and intermediate-term dermal endpoints were selected based on a submitted 21-day dermal toxicity study in rabbits.

A toxicity profile of technical oxamyl is presented in Table 1. The acute toxicity values for oxamyl are presented in Table 2.

Table 1: Toxicity Profile of Technical Oxamyl

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3200 21-Day dermal toxicity in rabbit	40827601 (1988) Acceptable/guideline 0, 2.5, 50 and 250 mg/kg/d (dermal 6 hrs/day) in ♂ and ♀	NOAEL = 2.5 mg/kg/day LOAEL = 50 mg/kg/day based on plasma, RBC and brain ChE inhibition **No clinical signs were observed.**
870.3200 21-Day dermal toxicity in rabbit	44751201 (1999) Acceptable/guideline 0, 25, 40, 50 and 75 mg/kg/d (dermal 6 hrs/day) in ♂ and ♀	NOAEL = 50 mg/kg/day for females and 75 mg/kg/day for males LOAEL = 75 mg/kg/day for females and > 75 mg/kg/day for males based on plasma, RBC and brain ChE inhibition
870.3700a Prenatal developmental in rodents	40859201 (1988) Acceptable/guideline 0, 0.2, 0.5, 0.8, & 1.5 mg/kg/d (gavage)	**Maternal** NOAEL = 0.5 mg/kg/day LOAEL = 0.8 mg/kg/day based on ↓ body wt. & food consumption and ↑ incidence of clinical signs associated with ChE inhibition (↑ tremors). **Developmental** NOAEL = 0.2 mg/kg/day LOAEL = 0.5 mg/kg/day based on decreased fetal body weights (not a developmental toxicant).
870.3700b Prenatal developmental in non-rodents	00063009 (1980) Acceptable/guideline 0, 1, 2, & 4 mg/kg/d (gavage)	**Materna**l NOAEL = 1 mg/kg/day LOAEL = 2 mg/kg/day based on decreased body wt. gains **Developmenta**l NOAEL = 4 mg/kg/day LOAEL = > 4 mg/kg/day (not a developmental toxicant)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800 Reproduction and fertility effects	41660801 (1991) Acceptable/guideline Doses: ♂ ♀ (mg/kg) 0 0 1.7 2.0 5.2 6.6 11.6 15.8	**Parental/Systemic** NOAEL = 1.7 mg/kg/day for males and 2.0 mg/kg/day for females LOAEL = 5.2 mg/kg/day for males and 6.6 mg/kg/day for females based on deceased food consumption, body weight, and body weight gain. In addition, at HDT hyperactivity, skin sores and alopecia. **Reproductive** NOAEL = 5.2 mg/kg/da for males and 6.6 mg/kg/day for females LOAEL = 11.6 mg/kg/day for males and 15.8 mg/kg/day for females based on decreased body weight during lactation. In addition, at HDT decreased number of live pups per litter during lactation and decreased viability index. **Offspring** NOAEL = 5.2 mg/kg/da for males and 6.6 mg/kg/day for females LOAEL = 11.6 mg/kg/day for males and 15.8 mg/kg/day for females based on decreased body weight during lactation. In addition, at HDT decreased number of live pups per litter during lactation and decreased viability index.
870.4100b Chronic toxicity dogs	41697901, 42052701 & 44737503 (1990-1999) Acceptable/guideline mg/kg/day ♂ ♀ 0 0 0.372 0.577 0.930 1.364 1.56 1.46 4.6 4.5 8 7.84	**Systemic** NOAEL = 1.56 mg/kg/day for males and 1.46 mg/kg/day for females LOAEL = 4.60 mg/kg/day for males and 4.50 mg/kg/day for females based on decreased body weights and body weight gains. **Cholinesterase** NOAEL = 0.930 mg/kg/day for males and 1.56 mg/kg/day for females LOAEL = 1.36 mg/kg/day for males and 4.50 mg/kg/day for females based on decreased brain cholinesterase levels in males and vomiting, tremors, plasma and brain ChE inhibition in females.
870.4200 Carcinogenicity rats	41963201 (1991) Acceptable/guideline mg/kg/day ♂ ♀ 0 0 0.992 1.32 1.97 2.69 4.19 6.73 6.99 11.1 Only plasma and red cell ChE was measured from 16 hr fasted rats	NOAEL = 1.97 mg/kg/day for males and 2.69 mg/kg/day for females LOAEL = 4.19 mg/kg/day for males and 6.73 mg/kg/da for females based on hyperactivity, swollen legs/paws, and skin sores, decreased body weights and body weight gains, increased incidence of ocular found in males and females and inhibition of plasma ChE in males. **No evidence of carcinogenicity**

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300 Carcinogenicity mice	00076813 (1981) Acceptable/guideline 0, 3.75, 7.5, 15/11.25 mg/kg/d	NOAEL = 3.75 mg/kg/day LOAEL = 7.5 mg/kg/day based on decreased body weights in males and mortality in males and females during initial phase of the study. **No evidence of carcinogenicity**
870.5100 Gene Mutation *Salmonella typhimurium* reverse gene mutation	40606509 (1981) Acceptable/guideline Doses: 50 to 10,000 μg/plate in the +/- of S9 activation	Negative in *S. typhimurium* strains TA1535, TA1537, TA98 and TA100.
870.5300 Gene Mutation CHO assay	40606510 (1982) Acceptable/guideline Doses: up to 1200 μM - S9 and up to 700 μM +S9	Test is negative in trials up to concentrations causing < 80% decrease in cell viability (1200 μM -S9; 700 μM +S9)
870.5375 Chromosomal aberration CHO cell chromosomal assay	40606507 (1982) Acceptable/guideline Doses: 700 μg +S9 to 70 μg/mL -S9 activation	Negative up to cytotoxic concentrations ($\leq$ 70 μg/mL -S9; 700 μg/mL +S9)
870.5500 Other genotoxic tests Bacterial DNA damage/repair	00049594 (1976) Acceptable/guideline Doses: up to 2000 μg/disc	Test was negative up to the highest dose tested.
870.5550 Other genotoxic tests Unscheduled DNA synthesis	40606508 & 41096001 (1982) Acceptable/guideline Doses: up to $\leq$ 5 mM	The test was negative up to cytotoxic concentrations.
870.6200a Acute neurotoxicity screening battery	44254401, 44420301 & 44740701 (1997) Acceptable/guideline Doses: mg/kg/day ♂ ♀ 0 0 0.1 0.1 1.0 0.75 2.0 1.5	NOAEL = 0.1 mg/kg/day LOAEL = 0.75 mg/kg/day for females and 1.0 mg/kg/day for males based on clinical signs, FOB effects, and decreased plasma, red blood cell and brain ChE activity.
870.6200b Subchronic neurotoxicity screening battery	44504901 (1998) Acceptable/guideline Doses: mg/kg/day ♂ ♀ 0 0 0.564 0.679 2.10 2.40 14.9 19.9	NOAEL = 2.10 mg/kg/day for males and 2.40 mg/kg/day for females LOAEL = 14.9 mg/kg/day for males and 19.9 mg/kg/day for females based on plasma, RBC and brain ChEI.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.7485 Metabolism and pharmacokinetics	41520801 (1990) Acceptable/guideline Doses: single oral dose of ^{14}C-oxamyl 1 mg/kg	With oral administration, oxamyl was readily absorbed and eliminated in the urine (80 - 91% of the dose) and feces (< 3% of the dose). The major component present in the urine was β-glucuronide of oxime (31 - 37% of the dose), followed by the metabolite oxime (13 - 18% of the dose) and the parent oxamyl (7 - 11% of the dose). No tissue accumulation was observed.

Table 2: Acute Toxicity Values of Technical Oxamyl

GDLN	Study Type	MRID	Results	Tox Category
81-1	Acute Oral	00063011	LD_{50} = 3.1 mg/kg (M); 2.5 mg/kg (F)	I
81-2	Acute Dermal (Rabbit)	40606501	LD_{50} > 5000 mg/kg (M) >2000 mg/kg (F) For abraded skin 90 mg/kg produced death with 50% a.i. in water	IV
81-3	Acute Inhalation	00066902	LC_{50} = 0.064 mg/L (4 hr) 0.17 mg/L (M) 0.12 mg/L (F) (I hr)	II
81-4	Primary Eye Irritation	00066984	Marked pupillary constriction, conjunctival irritation, reversible by 7 days	III
81-5	Primary Skin Irritation	00066900	Minor irritation was found at the application site. Severe systemic toxicity was seen after application on the abraded skin	IV
81-6	Dermal Sensitization	00006690	4/7 animals died (25% test material) 1/5 animals died (intradermal injection) Effects seen on the test site were slight. Extreme toxicity makes dermal sensitization study relatively unimportant	Not a skin sensitizer (25% test material)

GDLN	Study Type	MRID	Results	Tox Category
81-8	Acute neurotoxicity-hens 20 and 40 mg/kg as 1% suspension; the hens were protected with 0.5 mg/kg atropine. **Invalid study**	00066893	Clinical signs included: depression, lethargy, ruffled feathers, ataxia, incoordination, and slight respiratory difficulty. 12 hr. Later all symptoms disappeared. No compound-related histological changes were found. No deaths occurred.	NA

3.2 FQPA Considerations

On July 15, 1999, the FQPA Safety Factor Committee met to evaluate the hazard and exposure data for oxamyl, and recommended that the FQPA Safety Factor for the protection of infants and children be reduced to 1X for the following reasons (Memorandum: Report of the FQPA Safety Factor Committee, Brenda Tarplee, 09/13/99):

- Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

- A two generation reproduction toxicity study in rats showed no increased susceptibility in pups when compared to adults.

- There was no evidence of abnormalities in the development of fetal nervous system in the pre/post natal studies. Neither brain weight nor histopathology (perfused or non perfused) of the nervous system was affected in the subchronic and chronic toxicity studies.

- The toxicology data base is complete and there are no data gaps.

Based on the following weight-of-evidence considerations, the HIARC **did not recommend** a developmental neurotoxicity study in rats for oxamyl (Memorandum: Report of the Hazard Identification Assessment Review Committee, Guruva Reddy, 08/31/99):

- Clinical signs and FOB observations in acute and subchronic neurotoxicity studies were not associated with any neuropathology.

- Tremors seen in 1-year dog studies were not associated with any neuropathology. These signs may be due to cholinergic effects of oxamyl.

- Even though tremors were observed in the maternal animals in developmental rat study, there was no evidence of CNS malformations observed either in the rat or rabbit developmental toxicity studies.

- Even though hyperactivity was seen in 2-generation reproduction study, there was no apparent evidence of behavioral clinical observations in pups.

- The HIARC concluded that bilateral iris and retinal photoreceptor cell atrophy observed in female SD rats in a 2-year chronic study is likely due to aging of animals.

3.3 Endpoint Selection

On August 15, 1996, the HED's RfD Peer Review Committee established a reference dose (RfD) of 0.0002 mg/kg/day based on the NOAEL of 0.2 mg/kg/day established in the rat developmental toxicity study and an UF of 1000 for inter-species extrapolation, intra-species variation, and a lack of neurotoxicity studies (Memorandum: Rick Whiting, HED to Dennis Edwards, RD dated November 5, 1996).

On June 8, 1999 and July 15, 1999, the Hazard Identification Assessment Review Committee (HIARC) re-assessed the existing RfD and established the toxicology endpoints for acute dietary, chronic dietary, and occupational and residential exposure risk assessments pursuant to FQPA (Memorandum: Report of the Hazard Identification Assessment Review Committee, Guruva Reddy, 08/31/99).

The acute RfD of 0.001 mg/kg/day was derived from an acute neurotoxicity study in rats, and was calculated as the NOAEL (0.1 mg/kg/day) divided by an uncertainty factor of 100X (10X for interspecies extrapolation and 10X for intraspecies variability). The acute endpoint was based on clinical signs and plasma, red blood cell, and brain ChEI seen at the LOAEL of 0.75 mg/kg/day. Since the FQPA safety factor was reduced to 1X, the acute RfD is equal to the aPAD.

The chronic RfD of 0.001 mg/kg/day was derived from an acute neurotoxicity study in rats, and was calculated as the NOAEL (0.1 mg/kg/day) divided by the 100X UF. The chronic endpoint was based on clinical signs and plasma, red blood cell, and brain ChEI seen at the LOAEL of 0.75 mg/kg/day. Since the FQPA safety factor was reduced to 1X, the chronic RfD is equal to the cPAD.

Generally, a NOAEL/LOAEL from the chronic study is selected for establishing the chronic RfD. However, for oxamyl, the HIARC selected a NOAEL from an acute neurotoxicity study, based on weight of the evidence of the toxicity data, such as the chronic dog and rat studies which yielded a higher NOAEL/LOAEL compared to the acute neurotoxicity study. Since the measurement of ChEI was not conducted at the peak time in the chronic studies, the acute NOAEL (0.1 mg/kg) is also protective of any maternal/developmental effects. ChEI was reversible as determined in a carbamate reversibility study (i.e., no cumulative toxicity; recovery of clinical signs of ChEI and ChEI occurred within two hours post-dosing of 1 mg/kg oxamyl). Therefore, there is high confidence in the chronic RfD derived from the acute neurotoxicity study in the rat.

Two acceptable 21-day dermal toxicity studies in rabbits are available in the database. Although lower NOAELs for ChEI were observed in one study (MRIDs 408276-01 and 411182-01), this study was not used for the risk assessment because of uncertainty regarding the restraining of animals during the study. No dermal toxicity was observed in the second study (MRID 447512-01); however, systemic toxicity related to blood and brain ChEI was observed in females at the 75 mg/kg dose level.

Except for an acute inhalation toxicity study, no other inhalation studies are available. The short- and intermediate-term inhalation endpoints are based on the acute neurotoxicity study in the rat. Since the chronic dietary endpoint is also based on the acute neurotoxicity study in the rat, this study better predicts effects for inhalation exposure that is greater than one day.

The doses and toxicological endpoints selected for the various exposure scenarios are summarized in Table 3 below:

Table 3: Endpoints selected for risk assessment purposes

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	Acute Neurotoxicity NOAEL=0.1 UF=100	LOAEL = 0.75 mg/kg/day is based on clinical signs, and decreased plasma, red cell and brain cholinesterase inhibition in females	Acute Neurotoxicity - Rat
	Acute PAD (RfD) = 0.001 mg/kg		
Chronic Dietary	NOAEL=0.1 UF=100	LOAEL = 0.75 mg/kg/day is based on clinical signs, and decreased plasma, red cell and brain cholinesterase inhibition in females	Acute Neurotoxicity - Rat
	Chronic PAD (RfD) = 0.001 mg/kg/day		
Short- Term (Dermal) (1 to 7 days)	Dermal NOAEL=50 MOE=100	LOAEL = 75 mg/kg/day is based on plasma, red blood cell and brain ChEI in females	21-Day Dermal Toxicity - Rabbit
Intermediate- Term (Dermal) (one week to several months)	Dermal NOAEL=50 MOE=100	LOAEL = 75 mg/kg/day is based on plasma, red blood cell and brain ChEI in females	21-Day Dermal Toxicity - Rabbit
Long-Term (Dermal) (more than several months)	**Based on oxamyl's use pattern, this risk assessment is not required.**		
Inhalation (Short & Intermediate) (1 to 7 days and one week to several months)	Acute Neurotoxicity NOAEL=0.1 MOE=100 100% inhalation absorption assumed.	LOAEL = 0.75 mg/kg/day is based on clinical signs, and decreased plasma, red cell and brain cholinesterase inhibition in females	Acute Neurotoxicity - Rat
Inhalation (Long-Term) (more than several months)	**Based on oxamyl's use pattern, this risk assessment is not required.**		

4.0 EXPOSURE CHARACTERIZATION

4.1 Summary of Registered Uses

Oxamyl is a carbamate insecticide, acaricide, and nematicide that is applied preplant, at plant, postemergence, and foliarly on the following crops: apples, bananas, carrots, celery, citrus, cotton, cucumbers, eggplants, garlic, ginger, muskmelon (including cantaloupe and honeydew melon), onion (dry bulb), peanuts, pears, peppers, peppermint, pineapples, plantains, potatoes, pumpkins, soybeans, spearmint, squash, sweet potatoes, tobacco, tomatoes, watermelons, yams, and non-bearing apple, cherry, citrus, peach, and pear. Oxamyl is sold in the United States as a soluble concentrate under the trade name of Vydate® by E. I. du Pont de Nemours and Company (DuPont). The 2 and 3.77 lb/gallon liquid soluble concentrate formulations are the only oxamyl formulations registered for food/feed uses.

Oxamyl is applied with the following equipment: groundboom sprayer, aerial equipment, airblast sprayer, chemigation, spotgun applicator, seed piece dip, high pressure handwand, and shank soil injection. Application rates for oxamyl range from 0.25 to 8 lb ai/acre/day. Oxamyl can be applied from one to 12 times a year, depending on the crop. Most crops have a maximum seasonal application rate of 6 times a year or less. Current oxamyl labels state that oxamyl can only be used in commercial and farm planting. Current labels also specify that oxamyl is not for use in home planting, nor on any commercial crop that is turned into a "U-PICK," "PICK YOUR OWN," or similar operation.

4.2 Dietary Exposure

The tolerances for plant commodities listed in 40 CFR §180.303 are expressed in terms of the sum of the residues of oxamyl [methyl N',N'-dimethyl-N-((methylcarbamoyl)-oxy)-1-thiooxamimidate] and its oxime metabolite [N',N'-dimethyl-N-hydroxy-1-thiooxamimidate] calculated as oxamyl. The Agency notes that the oxime metabolite is listed incorrectly in 40 CFR §180.303, and should be listed as "methyl N',N'-dimethyl-N-hydroxy-1-thiooxamimidate." There are no toxicological concerns (no ChEI) for the oxime metabolite. Tolerances range from 0.1 ppm (potatoes and root crop vegetables) to 10 ppm (peppermint and spearmint hay, and pineapple forage). The established feed additive tolerance of 6 ppm for the processed food commodity, pineapple bran, is expressed in terms of oxamyl *per se* [40 CFR §186.4575]. No tolerances are currently established for oxamyl residues in animal commodities (meat, milk, poultry, and eggs).

The qualitative nature of the residue in plants is adequately understood based on studies with alfalfa, apples, beans, cotton, oranges, peanuts, potatoes, tobacco, and tomatoes. The residues to be regulated in plant commodities are oxamyl and its oxime metabolite (MARC decision memo dated 11/99, DP260911). The current tolerance expression for raw agricultural commodities is adequate; however, the tolerance expression for the established feed additive tolerance (40 CFR §186.4575) must be modified to include the oxime metabolite.

The qualitative nature of the residue in animals is adequately understood based on studies with lactating goats and laying hens. Oxamyl was found to be metabolized rapidly and extensively in goats and hens; oxamyl and its oxime metabolite were not detected in eggs, milk, or any tissue. The Agency has tentatively concluded that there is no reasonable expectation of finite oxamyl residues of concern in animal commodities [40 CFR §180.6(a)(3)]. However, this decision will be re-evaluated when residue data for cotton gin by-products are received and reviewed.

Adequate methods are available for data collection and tolerance enforcement for plant and animal commodities. The limit of quantitation is approximately 0.02 ppm. The Pesticide Analytical Manual (PAM) Vol. II lists a GLC method with flame photometric detection (sulfur mode), Method I, for the enforcement of tolerances for plant and animal commodities. This method involves alkaline hydrolysis to convert oxamyl to the oxime metabolite; therefore, the method determines combined residues of oxamyl and its oxime metabolite. Methods used for data collection are essentially the same as the PAM Vol. II method.

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that oxamyl is recovered (>80%) by Multiresidue Methods Section 302 (Luke Method; Protocol D) and Section 401. The registrant has conducted multiresidue methods trials with the oxime metabolite using Protocols C, D, and E. HED has forwarded the results of these multiresidue trials to FDA for evaluation and inclusion in PAM Vol. I, Appendix I. Radiovalidation of the method for meat, milk, poultry, or eggs was waived since no residues of oxamyl were found in exaggerated rate feeding studies.

Adequate storage stability data are available for residues of oxamyl and its oxime metabolite in/on root crop vegetables (onions and potatoes), leafy vegetables (celery and mint), fruits and fruiting vegetables (apples, cucumbers, oranges, pineapple, and tomatoes), and oilseeds and nuts (cottonseed, peanuts, and soybeans). Residues of oxamyl and its oxime metabolite were found to be stable for at least 24 months of frozen storage in/on these commodities, and residues of oxamyl *per se* were additionally found to be stable for at least 30 months in/on soybeans, and for at least 36 months in/on apples, celery, cottonseed, cucumbers, mint, onions, oranges, peanuts, potatoes, and tomatoes.

The reregistration requirements for magnitude of the residue in/on plants have been fulfilled for most commodities with tolerances. Adequate data are also available for processed plant commodities. The registrant is required to determine an appropriate tolerance level for cotton gin byproducts. The Agency does not expect this to-be-proposed tolerance to significantly alter any dietary assessment.

A summary of oxamyl tolerance reassessments can be found in the attached Residue Chemistry Chapter (J. Punzi memo, 03/07/00). The Agency recommends that established tolerances for peanut forage and hulls, pineapple forage, and soybean straw be revoked, as these items are no longer considered to be significant livestock feed items. A tolerance was originally established for the crop group "root crop vegetables" at 0.1 ppm; however, this tolerance will be revoked concomitant with establishment of individual tolerances for ginger, dry bulb onions, sweet potatoes, and yams. If the registrant or other interested party desires tolerances on any commodities for crop group 1, subgroup 1C or 1D, no additional field trial data would be required. A tolerance for cotton gin byproducts will be determined when magnitude of the residue data are received by the Agency.

Sufficient data are available to ascertain the adequacy of the established feed additive tolerance for pineapple bran, which has been redesignated as "processed pineapple residue." The available processing data indicate that the established tolerance can be reduced to 2 ppm concomitant with the revision in terminology.

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for oxamyl residues in various commodities (see *Guide to Codex Maximum Limits For Pesticide Residues, Part 2, FAO CX/PR, 4/91*). The Codex MRLs and U.S. tolerances are both expressed in terms of the sum of oxamyl and the oxime metabolite, and expressed as oxamyl. A comparison of the Codex MRLs and the corresponding **reassessed** U.S. tolerances shows that regarding efforts to harmonize the U.S. tolerances with the Codex MRLs: (I) compatibility between the U.S. tolerances and Codex MRLs exists for apple, carrots, cottonseed, cucumber, melons, peanut, peanut fodder, sweet peppers, pineapple, soya bean (dry), summer squash, tomato, and watermelon, and the root and tuber vegetables ginger, potatoes, yams, and sweet potatoes; and (ii) incompatibility of the U.S. tolerances and Codex MRLs remains for banana, celery, citrus fruits, and onion (bulb) because of differences in good agricultural practices. No questions of compatibility exist with respect to commodities where Codex MRLs have been established but U.S. tolerances do not exist or will be revoked.

4.2.1 Food Exposure

An acute and chronic dietary exposure analysis was conducted using the DEEM™ (Dietary Exposure Evaluation Model) exposure modeling software. DEEM™, developed by Novigen Sciences, Inc., calculates acute and chronic dietary risk estimates for the U.S. general population and various population subgroups. Food consumption data used in the software program are taken from the USDA Continuing Survey of Food Intake by Individuals (CSFII) for the years 1989-92. Consumption data are averaged for the entire U.S. population and population subgroups, such as “all infants,” to support chronic risk assessments, but are retained as individual daily consumption data points to support acute risk assessments (which are based on distributions of consumption estimates for either deterministic or probabilistic-type exposure estimates). The DEEM™ software is capable of calculating probabilistic-type risk assessments when appropriate residue data (distribution of residues) are available.

For acute risk assessments, one-day consumption data are summed and a food consumption distribution is calculated for each population subgroup of interest. The consumption distribution can be multiplied by a residue point estimate for a deterministic (Tier I/II) risk assessment, or used with a residue distribution in a probabilistic (Monte Carlo/Tier III) risk assessment. Exposure estimates are expressed in mg/kg bw/d and risks are expressed as a percent of the aPAD.

For chronic risk assessments, residue estimates for foods (e.g. apples) or food forms (e.g. apple juice) of interest are multiplied by the averaged consumption estimate of each food/food form for each population subgroup, based on consumption reported over three days. Exposure estimates are expressed in mg/kg bw/d and as percent of the cPAD.

Anticipated residues (ARs) used in the dietary risk assessment are calculated based primarily on three data sources: 1) USDA PDP food sampling data; 2) FDA surveillance monitoring data; and 3) field trial data, submitted primarily by the registrant for the purpose of tolerance assessment. For risk assessment purposes, the order of preference for these data are: PDP data > FDA data > field trial data. PDP data are preferred over FDA data because the statistical design of the PDP program is specific for dietary risk assessment (i.e., sampling is done at grocery store distribution points instead of directly from the field) and because the foods are prepared closer to the point of consumption (i.e., washing and peeling). Field trial residue data are considered by the Agency as an upper-end, or worst case, scenario of possible residues, and are more suited to the requirements of tolerance setting than to the requirements of dietary risk assessment.

USDA PDP monitoring data generally show oxamyl to be present in/on only a few crops at relatively low levels. However, PDP has found significant residues of oxamyl in/on celery and apple, ranging from 0.017-0.28 ppm for celery and 0.014-0.32 ppm for apples. Apple juice, green beans, spinach, tomatoes, pears, cantaloupe, and winter squash also show residues above the Level of Detection (LOD); however, the frequency of occurrence in/on these crops was <1%. PDP monitoring data samples for the parent oxamyl only. The oxime metabolite is not of toxicological concern.

FDA monitoring data for oxamyl also show residues present on only a few crops at relatively low levels. Oxamyl was found in/on honeydew, squash, watermelon, eggplant, sweet and hot pepper, pears, and apples. Apples, pears, and peppers consistently demonstrated detectable residues from year to year, with values ranging from 0.003-0.089 ppm for apples, 0.003-0.11 ppm for cantaloupe, and 0.003-0.61 ppm for sweet pepper. FDA monitoring data distinguishes between parent oxamyl and its metabolite oxime.

The PDP and FDA databases report the majority of detected residues as residues found in 5 lb. (PDP) and 20 lb. (FDA) composite samples. This manner of reporting may not be representative of possible high-end residues that could be found if individual units of fruits and vegetables were analyzed. This assessment uses statistical methodology for applying existing (composite) information to acute dietary risk assessments. This methodology consists of extrapolating data on pesticide residues in composite samples of fruits and vegetables to residue levels in single servings of fruits and vegetables. Given the composite sample mean**,** the composite sample variance, the number of units in each composite sample, and assuming a lognormal distribution, it is possible to *estimate* the mean and variance of the pesticide residues present on single servings of fruits and vegetables. These parameters can then be applied to generate information on the level of residue in fruits and vegetables (and calculate a theoretical distribution). This information was incorporated into a probabilistic exposure estimation model, the Monte-Carlo method. This methodology has a higher degree of accuracy when more than 30 composite samples have detectable residues (Use of Pesticide Data Program in Acute Risk Assessment - sent to Federal Register May, 1999). Commodities that are blended (such as grains) or are smaller than single unit servings (peas) are not decomposited since the measured PDP levels are assumed to be representative of the actual range of residue.

Field trial data were used for cottonseed, eggplant, ginger, garlic, onions, peanuts, mint, and pineapple. Since it is presently not possible to estimate the ratio of oxamyl to oxime from these field trials, residues in/on these commodities were assumed to be entirely oxamyl, and consequently very conservative.

Oxamyl residues may be either concentrated or reduced by activities such as drying (dried fruits), processing (juice, catsup, etc.), washing, peeling, and cooking. Processing factors for cottonseed, soybean, tomatoes, and pineapple were incorporated into the dietary assessment for oxamyl.

Residue reduction due to processing was also obtained from studies of methomyl degradation on apples (baking) and green beans (canning). Since methomyl and oxamyl are structurally related, it is likely that oxamyl will degrade in a similar fashion. Furthermore, HED believes that the degradation of these two carbamates by the process of baking and/or canning will result in the formation of compounds that are unlikely to be potent cholinesterase inhibitors. These reduction factors were applied to all "baked" and "canned" food forms. Default processing factors were used in all other cases.

At the present time the preliminary information from the industry-sponsored Carbamate Marketbasket Survey is not appropriate for use in dietary risk assessments in RED documents. The amount of data currently available from the survey is insufficient for meaningful analysis, and quality assurance procedures have not been completed. When sufficient data have been collected and quality assurance procedures completed, the Agency will examine the database for appropriateness of inclusion into dietary risk assessments for the carbamate pesticides monitored in the study.

4.2.1.1 Acute Dietary Exposure Assessment

A highly refined, Tier 3 acute probabilistic dietary exposure analysis was conducted for oxamyl, incorporating percent crop treated information from the Biological and Economic Analysis Division (BEAD), PDP and FDA monitoring data, and field trial data. For the revised dietary risk assessment, anticipated residue estimates for pineapple and apple, and processing factors for baked and canned food forms were reassessed based on information provided by the registrant, the Pineapple Growers Association, and preliminary, single serving, residue monitoring results from the 1999 USDA PDP data. At the 99.9th percentile, acute dietary risk estimates are below the Agency's level of concern (<100% of the aPAD) for all population subgroups. Children (1-6 years old) are the highest exposed population subgroup at 81% of the aPAD.

Acute dietary risk estimates are summarized in Table 4 below.

Table 4: Tier 3 Acute Dietary Risk Estimates at the 99.9th percentile

Population	Acute Dietary	
	Exposure (mg/kg/d)	% aPAD
U.S. population	0.000433	43
All infants (<1 year)	0.000382	38
Children (1-6 years)	0.000807	81
Children (7-12 years)	0.000412	41
Females (20+ years))	0.000391	39
Males (13-19 years)	0.000230	23
Males (20+ years)	0.000321	32

4.2.1.2 Chronic Dietary Exposure Assessment

Inputs to the DEEM chronic analysis include reassessed tolerances, percent crop treated information, and monitoring data. Reported residues were averaged, whether based on PDP, FDA, or field trials. If a commodity had no reported detections by the PDP and FDA programs, and the expectation of no detection was confirmed by field trial data, the weighted average of the LOD was used to account for possible exposure that could not be more precisely quantified. The weighted average estimate of the percent crop treated was incorporated into all chronic residue estimates. Risk estimates for all population subgroups are below the Agency's level of concern (<100% cPAD). Children (1-6 years old) are the highest exposed population subgroup at 12% of the cPAD.

Chronic dietary risk estimates for oxamyl are summarized in Table 5 below.

Table 5: Tier 3 Chronic Dietary Risk Estimates

Population	Chronic Dietary	
	Exposure (mg/kg/d)	%PAD
U.S. population	0.000043	4
All infants (<1 year)	0.000112	11
Children (1-6 years)	0.000121	12
Children (7-12 years)	0.000061	6
Females (20+ years)	0.000034	3
Males (20+ years)	0.000026	3

4.2.2 Drinking Water Exposure

The Environmental Fate and Effects Division (EFED) has provided a refined Tier 2 surface water and a Tier 1 groundwater analysis for the parent oxamyl, using computer modeling and existing monitoring data (E. Libelo memo; 10/28/99). Estimated environmental concentrations (EECs) for oxamyl were calculated using PRZM/EXAMS (Tier 2 surface water) and monitoring data from the United States Geological Survey (USGS) National Water Quality Assessment Program (NAWQA) and the STORET database. The limit of detection for the USGS monitoring data is 0.018 ppb.

The environmental fate database for oxamyl is adequate to characterize drinking water exposure. Parent oxamyl has a low affinity for adsorption, and is highly mobile in a variety of soils. Field dissipation and prospective groundwater studies show that both oxamyl and oxime are capable of leaching through the soil.

EEC's are based on the parent oxamyl only. HED's Metabolism Assessment Review Committee has determined that the metabolite (oxime) is not likely to be a potent acetyl cholinesterase inhibitor.

Surface Water: For drinking water originating in surface water bodies, an **acute** concentration of 1 μg/L was used to evaluate the risk to human health. This value is slightly higher than maximum concentrations (0.7 μg/L) reported in monitoring studies, but significantly lower than the conservative PRZM/EXAMS simulation results (30 μg/L). A value of 1 μg/L represents an upper bound on potential peak concentrations of oxamyl that can be expected in drinking water. A **chronic** concentration of 0.3 μg/L was used to evaluate the risk to human health. This value is based on the 1-in-10 year average annual concentration calculated using PRZM/EXAMS, and is in accordance with observed monitoring data. PRZM/EXAMS only models for the parent oxamyl.

Groundwater: For drinking water derived from groundwater, an **acute** concentration of 4 μg/L was used to evaluate the risk to human health. This value is based on typical maximum values observed in non-targeted and prospective groundwater (PGW) monitoring studies, and represents parent oxamyl only. Although higher groundwater concentrations have been reported in some monitoring studies, these are not typical results and most likely represent extremely vulnerable areas. A **chronic** concentration of 1 μg/L was used to evaluate the risk to human health. This value is fairly conservative and is based on typical concentrations observed in monitoring studies where the parent compound was detected.

Surface and groundwater monitoring data: Oxamyl is generally not found at high levels in surface water monitoring samples. Oxamyl was only detected in one sample out of 5,200 in the USGS National Assessment of Water Quality study, and only 14 detections were reported from the STORET database. Concentrations ranged from 0.07 μg/L to 0.7 μg/L. These data do not reflect source-to-tap dilution, nor do they reflect drinking water treatment. USGS and STORET do not monitor for the oxime; they only monitor for the parent oxamyl. Under acidic conditions, the half-life of oxamyl is 1-2 weeks, and under alkaline conditions, oxamyl hydrolyzes to the oxime within hours, further decreasing the likelihood that oxamyl will be found "at the tap" at any measurable levels.

Evidence suggests that oxamyl does have the potential to leach to groundwater. The U.S. EPA Pesticides in Groundwater Database reports 907 detections out of 23,305 groundwater well samples between 1971-1991. Concentrations ranged from 0.01 μg/L to 395 μg/L. The majority of the detections were in Suffolk County, New York, with only three of 894 wells sampled showing detections above 70 μg/L, with the maximum concentration reported being 395 μg/L. In the USGS NAWQA studies, oxamyl was not detected in groundwater samples above the detection limit (0.018 ppb) in any of the 3,144 samples analyzed. Smaller-scale, non-targeted monitoring studies in the New Jersey coastal plain, North Carolina, and Mississippi show that oxamyl was not detected in groundwater, or was detected very infrequently and at very low levels.

The EPA requested that Small Scale Prospective Groundwater (PGW) Monitoring studies be conducted in order to determine the potential impact of oxamyl on ground water. These studies have shown that parent oxamyl was detected in groundwater at concentrations up to 4 ppb, but generally the concentration was below 1 ppb. The oxime degradate was detected at concentrations up to 4.5 ppb and concentrations of 1-2 ppb were common for several hundred days. The degradate appeared to be significantly more persistent than the parent. Tier 1 groundwater modeling results (based on SCI-GROW) are in accordance with groundwater concentrations observed in monitoring studies.

Drinking Water Levels of Comparison (DWLOCs): A DWLOC is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. The Office of Pesticide Programs (OPP) uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. DWLOC values are not regulatory standards for drinking water; however, they do have an indirect regulatory impact through aggregate exposure and risk assessments.

4.2.2.1 DWLOCs for Acute Exposure

Acute DWLOCs were calculated for oxamyl based on acute dietary food exposure and default body weight and water consumption figures. The default body weights and daily water consumption values used to calculate DWLOCs are as follows: 70 kg/2 L (adult male), 60 kg/2 L (adult female), and 10 kg/1 L (children and infants). To calculate the acute DWLOC, the following equation was used:

$$DWLOC_{acute} = \frac{[\text{allowable acute water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3} \text{ mg/}\mu\text{g}]}$$

where allowable acute water exposure (mg/kg/day) = [aPAD - acute food (mg/kg/day)].

As shown in Table 6 below, EFED's estimated environmental concentrations of oxamyl residues in surface and ground water are below the Agency's back-calculated DWLOCs for all population subgroups of concern, with the exception of residues in ground water for children 1-6. Acute exposure to residues of oxamyl in ground water may be a risk of concern for children 1-6.

Table 6: Drinking Water Levels of Comparison for Acute Dietary Exposure

Acute Surface and Ground Water

Population	PRZM/EXAMS (μg/L)	Ground Water Monitoring data (μg/L)	aPAD (mg/kg/d)	Acute Food Exposure (mg/kg/d)	Allowable Acute Water Exposure (mg/kg/d)	$DWLOC_{acutec}$ (μg/L)
U.S. Population	1.0	4.0	0.001	0.000433	0.000567	20
Children (1-6)	1.0	4.0	0.001	0.000807	0.000193	1.9
Females (20+)	1.0	4.0	0.001	0.000391	0.000609	18

4.2.2.2 DWLOCs for Chronic Exposure

Chronic DWLOCs were calculated for oxamyl based on chronic dietary food exposure and default body weight and water consumption figures. The default body weights and daily water consumption values used to calculate DWLOCs are as follows: 70 kg/2 L (adult male), 60 kg/2 L (adult female), and 10 kg/1 L (children and infants). To calculate the chronic DWLOC, the following equation was used:

$$DWLOC_{chronic} = \frac{[\text{allowable chronic water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3} \text{ mg/}\mu\text{g}]}$$

where allowable chronic water exposure (mg/kg/day) = [cPAD - chronic food (mg/kg/day)].

As shown in Table 7 below, EFED's estimated environmental concentrations of oxamyl residues in surface and ground water are below the Agency's back-calculated DWLOCs for all population subgroups of concern. Chronic exposure to residues of oxamyl in surface and ground water is below the Agency's level of concern.

Table 7: Drinking Water Levels of Comparison for Chronic Dietary Exposure

Chronic Surface and Ground Water						
Population	**PRZM/EXAMS (μg/L)**	**Ground Water Monitoring data (μg/L)**	**cPAD (mg/kg/d)**	**Chronic Food Exposure (mg/kg/d)**	**Allowable chronic Water Exposure (mg/kg/d)**	**$DWLOC_{chronic}$ (μg/L)**
U.S. Population	0.3	1	0.001	0.000043	0.000957	33

Chronic Surface and Ground Water						
Children (1-6)	0.3	1	0.001	0.000121	0.000879	8.8
Females (13-50)	0.3	1	0.001	0.000034	0.000966	29

4.3 Occupational Exposure

The Agency has determined that occupational exposure to oxamyl residues via the dermal and inhalation routes of exposure may occur during mixing, loading, applying, and other handler-use activities. In addition, the Agency has determined that there is potential dermal exposure to post-application occupational workers for usual use-patterns associated with oxamyl.

The PPE required for handlers by current oxamyl labels includes: coveralls over short sleeved shirt and short pants, chemical resistant gloves, such as barrier laminate, butyl rubber, neoprene rubber, polyvinyl chloride, viton or nitrile gloves, chemical resistant footwear plus socks, protective eye wear, chemical resistant head wear for overhead exposure, chemical resistant apron when cleaning equipment, mixing or loading, and a respirator with an organic vapor cartridge with a pre-filter approved for pesticides, a canister approved for pesticides, or a NIOSH approved respirator with an organic vapor cartridge or canister with any R, P, or HE pre-filter. The engineering control required for handlers by current oxamyl labels is the use of an enclosed cab for human flaggers.

The current oxamyl label reentry interval (REI) is 48 hours. The PPE required on current oxamyl labels for early entry that involves contact with anything that has been treated, such as plants, soil or water, is: coveralls over short-sleeved shirt and short pants, chemical resistant gloves, such as barrier laminate, butyl rubber, neoprene rubber, polyvinyl chloride, viton or nitrile gloves, chemical resistant footwear plus socks, protective eye wear, and chemical resistant head wear for overhead exposure.

4.3.1 Occupational Handler Exposure Scenarios

Based on registered use patterns, eight major exposure scenarios were identified for oxamyl: (1a) mixing/loading liquids for aerial application; (1b) mixing/loading liquids for groundboom application; (1c) mixing/loading liquids for airblast application; (1d) mixing/loading liquids for spotgun applicator; (1e) mixing/loading liquids for high pressure handwand; (2) applying liquids with aerial equipment; (3) applying liquids with a groundboom sprayer; (4) applying liquids with an airblast sprayer; (5) applying liquids for spotgun treatment; (6) applying liquids with a high pressure handwand; (7) mixing/loading/applying liquids by seed piece dip; and (8) flagging for liquid aerial applications.

These scenarios are of short-term (1-7 days) and intermediate-term (1 week to several months) duration only, and represent a broad range of application equipment, application methods, and use sites. No chronic occupational scenarios were identified for oxamyl. The estimated exposures considered baseline protection (long pants, long sleeved shirt, no gloves, open mixing/loading, open cab tractor), additional PPE (double layer of clothing, chemical resistant gloves, and an organic vapor respirator), and engineering controls (closed mixing/loading and enclosed cab, cockpit, and truck).

4.3.2 Occupational Handler Exposure Data Sources and Assumptions

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of the reregistration of oxamyl. It is the policy of the Agency to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical specific monitoring data are not available. PHED is a software system consisting of two parts: a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). While data from PHED provides the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. Overall, there is medium to high confidence in the PHED data from which the occupational exposure assessment was derived.

General assumptions used in the occupational exposure assessment include an average body weight of an adult handler as 70 kg and an average work day interval of eight hours, which represents the acres treated or volume of spray solution prepared in a typical day. Calculations of handler scenarios are completed using the maximum application rates on the available oxamyl labels. Exposures were estimated for handlers using 1200 acres per day for aerial equipment and chemigation on cotton, since it is a large acre crop, and 350 acres per day for aerial equipment, flaggers, and chemigation on field and tree crops, 40 acres per day for airblast sprayers on tree crops, 1000 gallons for a high pressure handwand, and 1 acre per day for a spotgun applicator. For groundboom equipment use on cotton, since it is a large acre crop, a range of 200 acres per day (upper-end estimate) to 80 acres per day (typical estimate) was used. For all other groundboom equipment uses, 80 acres per day was used. Since exposure from shank injection application on tomatoes and celery is considered to be similar to groundboom applicator exposure (scenario 4), the shank injection application method was assessed under the groundboom scenario. This is a conservative estimate of the exposure since the application rates are lower, the acres treated per day is lower, and the spray is released in-ground.

4.3.3 Occupational Handler Risk Characterization

Dermal and inhalation NOAELs were based on identical effects of plasma, red blood cell, and brain ChEI; therefore, the dermal and inhalation MOEs were combined to determine a total short-term MOE and a total intermediate-term MOE. The target MOE for all scenarios is 100. A MOE greater than or equal to 100 is considered to be *below* the Agency's level of concern; a MOE of less than 100 is considered to be *above* the Agency's level of concern. A summary of the total short- and intermediate-term risk estimates for baseline, additional PPE, and engineering controls is presented in Appendix 1.

All calculated short- and intermediate-term total MOEs were above the Agency's level of concern (MOE $\leq$ 100) at the baseline level (long pants, long sleeved shirt, no gloves, open mixing/loading, open cab tractor) **except** for the following:

- (1d) Mixing/loading liquids for spotgun applicator.

- (4) Applying liquids with a groundboom sprayer on cotton (1 lb ai/acre) at 80 acres per day.

Calculated short- and intermediate-term total MOEs were below the Agency's level of concern (MOE $\geq$100) at the additional PPE level (double layer of clothing, chemical resistant gloves, and an organic vapor respirator) for all assessed exposure scenarios **except** for the following:

- (1a) Mixing/loading liquids for aerial and chemigation application for all application rates.

- (1c) Mixing/loading liquids for groundboom application for the highest application of 8 lbs ai/acre.

- (3) Applying liquids with airblast equipment at all application rates.

- (5) Applying liquids with a spotgun applicator (not able to mitigate with engineering controls).

- (6) Applying liquids with a high pressure handwand (not able to mitigate with engineering controls).

Calculated short- and intermediate-term total MOEs were below the Agency's level of concern (MOE $\geq$100) at the engineering control level for all assessed exposure scenarios **except** for the following:

- (1a) Mixing/loading liquids for aerial and chemigation application for all application rates.

- (2) Applying liquids with aerial equipment for all application rates.

In summary, the following four exposure scenarios are above the Agency's level of concern (MOE $\leq$100) at the highest level of risk mitigation: (5) applying liquids with a spotgun applicator (cannot be mitigated with engineering controls; MOE = 63), (6) applying liquids with a high pressure handwand (cannot be mitigated with engineering controls; MOE = 41), (1a) mixing/loading liquids for aerial and chemigation application at all application rates (MOEs range from 50-66), and (2) applying liquids with aerial equipment for all application rates (MOEs range from 75-85). There are no available data to assess the exposure scenario mixing/loading/applying liquids by a seed piece dip (scenario 7). Table 8 presents a summary of total short- and intermediate-term occupational risk concerns at baseline, with PPE, and engineering controls.

Table 8: Summary of Total Short- and Intermediate-Term Occupational Risk Concerns for Oxamyl at Baseline, with PPE, and Engineering Controls

Exposure Scenario (Scenario #)	Short- and Intermediate Term MOE = 100		
	Baseline	PPE	Engineering Controls
LOADER EXPOSURE			
Mixing/Loading liquids for aerial application/chemigation (1a)	0.7-1	32-43	50-66
Mixing/Loading liquids for airblast application (1b)	13	570	–[2]
Mixing/Loading liquids for groundboom application (1c)	2-13	71-570	110
Mixing/Loading liquids for spotgun applicator (1d)	500	--	--
Mixing/loading liquids for high pressure handwand (1e)	50	2,300	--
APPLICATOR EXPOSURES			
Applying liquids with aerial equipment (2)	see eng. controls	see eng. controls	75-85
Applying liquids with airblast equipment (3)	17	98	180
Applying liquids with groundboom sprayer (4)	14-120	110-370	--
Applying liquids with a spotgun applicator (5)	15	63	N/A[3]
Applying liquids with a high pressure handwand (6)	4	41	N/A
MIXER/LOADER/APPLICATOR EXPOSURES			
Mixing/Loading/Applying liquid by seed piece dip (7)	no data	no data	N/A
FLAGGER EXPOSURE			
Flagging liquid applications (8)	18-54	120-360	–

4.3.4 Occupational Postapplication Exposure

The Agency has determined that there is a potential for dermal exposure to post-application workers during usual use-patterns associated with oxamyl. The registrant has submitted three

[2] Calculated MOEs are below HED’s level of concern at the previous level of mitigation (total MOE ≥100).

[3] Not applicable–the Agency does not consider engineering controls an effective approach for mitigating exposures during the use of certain types of equipment.

dislodgeable foliar residue (DFR) studies to the Agency in support of the reregistration of oxamyl. The dissipation data obtained from these studies will be used to determine the re-entry interval (REI) for all oxamyl crops. See Appendix 1 in the Revised Occupational Exposure and Risk Assessment chapter (R. Sandvig memo, 03/24/00) for the raw data from the three dissipation studies. The raw data from the studies are corrected for recoveries as appropriate. The data is then natural log transformed. A semi-log regression analysis is run on the log transformed data. From the regression analysis, a dissipation rate (slope) and predicted dislodgeable foliar residue data for each site and crop is determined. The REI is generally established on the day that the calculated MOE is 100 or above.

The DFR studies were conducted on cucumbers, tomatoes, and citrus fruits. Two sites were chosen for each crop: one in California, and one is Florida or Georgia, to represent one arid and one non-arid climate. A soil residue study was conducted at the California site on tomato plants.

The following assumptions were used in calculating the REIs. The transfer coefficients used are standard Agency default values.

- The transfer coefficient used for exposure to cucurbits, ginger, peanuts, cotton, pepper, and eggplant foliage was 4,000 cm^2/hr from activities such as hand harvesting, scouting, staking/tying, and irrigating.

- The transfer coefficient used for exposure to celery and pineapple foliage was 2,500 cm^2/hr from activities such as hand harvesting.

- The transfer coefficient used for exposure to citrus, pear, apple, and non-bearing trees was 10,000 cm^2/hr from activities such as hand harvesting, transplanting, and pruning.

- The transfer coefficient used for exposure to tomatoes, yams, white potatoes, garlic, and onions was 10,000 cm^2/hr from activities such as staking/tying, irrigating, hand harvesting, and digging.

- A route-specific dermal study was used to select an endpoint, so a dermal absorption value is not necessary.

- The exposure duration is assumed to be an eight hour work day.

- Adult body weight is 70 kg.

Although the DFR studies contained several omissions and flaws with respect to the Series 875 Group B Postapplication Exposure Monitoring Test Guidelines, the Agency has determined that the collected data are of sufficient scientific quality.

For crops other than tomatoes, cucumbers, and citrus, the target MOE of 100 is reached using the DFR data as surrogate data. The citrus residue data were used to assess exposure to foliage from the tree crops (pears, apples, and non-bearing trees); tomato residue data were used to assess exposure to foliage from yams, white potatoes, garlic, and onion; and cucumber residue data were used to assess exposure to foliage from ginger, cucurbits, peanuts, cotton, peppers, eggplant, celery, and pineapples. The DFR values from the three submitted studies were adjusted proportionately to reflect the remaining crops' application rates.

The results of the postapplication exposure assessment are presented in Table 9.

Table 9: Summary of the Day After Application When MOEs ≥ 100

Crop	Activity and Transfer Coefficient (cm^2/hr)	Application Rate (lbs ai/A)	Day after Application When MOE ≥100	
			FL/GA	CA
Citrus Trees	10,000 - hand harvesting and pruning	1	3	7
Pear and Apple	10,000 - hand harvesting and pruning	2	5	16
Non-bearing Fruit Trees	10,000 - transplanting, pruning, and hand harvesting	2	5	16
Cucumbers, ginger, cucurbits, peanuts, cotton, peppers, and eggplant	4,000 hand harvesting, scouting, irrigating, staking/tying	1	1	4
Celery	2,500 - hand harvesting	1	1	3
Pineapples	2,500 - hand harvesting	2	1	5
Tomatoes	10,000 - hand harvesting, staking/tying, irrigating	1	4	3
True Yams	10,000 - hand harvesting and digging	0.5	2	2
White Potatoes, garlic, and onions	10,000 - hand harvesting and digging	1	4	3

4.4 Residential Exposure

There are no registered residential uses of oxamyl. Therefore, a residential handler and postapplication assessment was not conducted. However, the Agency does have concerns about possible residential risks from oxamyl spray drift. The Agency is currently developing methods to assess residential risks from spray drift, and these risks will be assessed in the future when appropriate methodologies are available.

4.5 Incident Reports

Poisoning incident data are available for oxamyl from the following data bases: OPP Incident Data System (IDS), Poison Control Centers, California Department of Pesticide Regulation, and the

National Pesticide Telecommunications Network (NPTN). A review of published data indicate that the activities in which workers were most frequently engaged during their exposures to oxamyl were coincidental exposure (exposure while working but not assigned to deal with pesticides) and pesticide application. Compared to the most toxic organophosphate and carbamate pesticides evaluated in the acute Worker Risk Strategy, oxamyl has a similar ratio of incidents per amount of use. However, these data are based on far fewer cases and very limited usage (Memorandum: Oxamyl–Review of Pesticide Poisoning Incident Data, Virginia Dobozy, 10/01/96).

5.0 AGGREGATE RISK ASSESSMENT

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require that for establishing a pesticide tolerance "that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information." Aggregate exposure will typically include exposures from food, drinking water, and residential uses of a pesticide. Aggregate risk assessments are conducted for acute (1 day), short-term (1-7 days), intermediate-term (7 days to several months), and chronic (lifetime) exposure. Occupational exposure is not considered in any aggregate exposure assessment.

5.1 Acute Aggregate Risk

The aggregate acute dietary risk estimates include exposure to oxamyl in food and water and do not include dermal, inhalation, or incidental oral exposure.

Acute dietary food risks are below the Agency's level of concern. The estimated concentration of oxamyl in drinking water as a contribution to acute aggregate risk is below HED's level of concern, with the exception of children 1-6 years old.

Based on the available information, the Agency concludes that residues of oxamyl in drinking water (when considered along with exposures from food uses) may result in an unacceptable acute aggregate human health risk estimate.

5.2 Short-term Aggregate Risk

A short-term aggregate risk assessment was not conducted for oxamyl. There are no short-term residential scenarios of concern.

5.3 Intermediate-term Aggregate Risk

An intermediate-term aggregate risk assessment was not conducted for oxamyl. There are no intermediate-term residential scenarios of concern.

5.4 Chronic Aggregate Risk

The chronic aggregate risk estimate to oxamyl addresses exposure from food and drinking water. Chronic dietary food risks are below the Agency's level of concern. The estimated concentration of oxamyl in ground water and surface water is below the Agency's level of concern for exposure to oxamyl in drinking water as a contribution to chronic aggregate risk.

Based on the available information, the Agency concludes with reasonable certainty that residues of oxamyl in drinking water (when considered along with exposures from food uses) would not result in an unacceptable chronic aggregate human health risk estimate.

6.0 DEFICIENCIES / DATA NEEDS

Additional data requirements for oxamyl are identified as follows:

<u>Product Chemistry data gaps:</u>

830.1600 Description of Materials Used to Produce the Product.
830.7050 UV/Visible Absorption.

<u>Residue Chemistry data gaps:</u>

860.1200 Directions for Use[4]
860.1500 Crop Field Trials (Cotton Gin Byproducts)[5]

<u>Occupational Exposure data gaps:</u>

There are no available data to assess the scenario mixing/loading/applying liquids by seed piece dip. An exposure study done in conjunction with soil residue data collection to determine the transfer rate of the pesticide from the treated soil to the worker may be required pending the outcome of discussions with the registrant and others on the postapplication risk and risk mitigation.

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[4]Label modifications are required to reflect the use patterns for which adequate field residue data are available. These required label modifications are specified in the text under "Directions for Use".

[5]As a result of changes in Table 1 of OPPTS 860.1000 (7/31/96), the Agency now considers cotton gin byproducts to be a raw agricultural commodity (RAC). Data depicting oxamyl residues of concern in/on cotton gin byproducts resulting from the maximum registered use of oxamyl on cotton are required. Cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue for the ginning process. At least 3 field trials for each type of harvesting (stripper and picker) are required, for a total of 6 field trials.

7.0 ATTACHMENTS

Review of Pesticide Poisoning Incident Data. Virginia Dobozy; 10/01/96. D229743.
Revised Product Chemistry Chapter for the Reregistration Eligibility Decision (RED) Document. Ken Dockter; 03/15/00. D263858.
Report of the Hazard Identification Assessment Review Committee. Guruva Reddy; 8/31/99.
Report of the FQPA Safety Factor Committee. Brenda Tarplee; 9/13/99.
Revised Toxicology Chapter for the RED. Guruva Reddy; 03/31/00. D263844.
Tier II Estimated Environmental Concentrations for Oxamyl. E. Laurence Libelo; 10/28/99. D259661.
Revised Residue Chemistry Chapter for the Oxamyl Reregistration Eligibility Decision (RED) Document. John S. Punzi; 03/07/00. D263849.
Revised Anticipated Residue and Dietary Exposure Estimates. John S. Punzi; 03/09/00. D263853.
Revised Occupational Exposure and Risk Assessment Regarding the Use of Oxamyl. Renee Sandvig; 03/17/00. D263856.